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EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,290	HOLTET ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,18-23,30 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,18-23,30 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/7/06, 11/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 73 (claims 1-8, 18, monomer of amino acid sequence set forth in SEQ ID NO:106) in the reply filed on 6/6/08 is acknowledged. The traversal is on the ground(s) that the restriction is improper because there will be no undue hardship on the Office in performing a search with respect to the amino acid sequences of SEQ ID NOs: 106, 107, and 108, Exhibit A illustrates that all three of these sequences share substantial sequence identity and similarity. In particular, the sequence of SEQ ID NO: 106 differs from the sequences of SEQ ID NO: 107 and 108 at only position 166, the sequence of SEQ ID NO: 107 differs from the sequences of SEQ ID NO: 106 and 108 at only position 147, and the sequence of SEQ ID NO: 108 differs from the sequences of SEQ ID NO: 106 and 107 at only positions 125 and 149, other than these four differences, the three sequences are 100% identical and Applicants contend that a search with respect any one of these amino acid sequences would uncover all art pertinent to the other amino acid sequences. Applicants arguments are found persuasive and claims corresponding to SEQ ID NO:106, 107, 108, will be examined in the instant application.

Claims 2-17, 24-29, 31-34 have been canceled (6/6/08). Amended claims 1, 18-22, 35 (7/16/08) and previous claims 23, 30 are pending and under consideration by the Examiner.

Claim Rejections - 35 U.S.C. § 112, first paragraph, written description

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 1, 18-23, 30, 35, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 18 recites "at least 87% identity" with a particular disclosed sequence (SEQ ID NO:81 of 51 amino acids) and claim 19 recites "at least 92% identity" with a particular disclosed sequence (SEQ ID NO:81). The claims do not require that the polypeptide possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is the ability to induce proliferation or development of lymphocytes. There is not even identification of any particular portion of the structure that must be conserved for the desired biological activity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics and structure/function relationship, the specification does not provide adequate written description of the claimed genus of peptides.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the ad that, as of the filing date sought, he or she was in

possession *of the invention*. The invention is, for purposes of the written description' inquiry, whatever is *now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only a tetranectin trimerising domain comprising the amino acid sequence set forth in SEQ ID NO:81, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

With the exception of the tetranectin trimerising domain of SEQ ID NO:81, the skilled artisan cannot envision the polypeptide as recited in claims 18 and 19 and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the protein. Adequate written description requires more than a mere statement that it is part of

the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for only the tetranectin trimerising domain polypeptide of SEQ ID NO:81 has been provided in the instant specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore, only a trimeric polypeptide comprising three monomers wherein each monomer comprises the amino acid sequence set forth in SEQ ID NO:106 and comprises a cytokine binding domain and a tetranectin trimerising domain polypeptide of SEQ ID NO:81, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Furthermore claims 1, 18 and 19 are genus claims. Claim 1 encompasses all monomers comprising a cytokine binding domain and a tetranectin trimerising domain. However, the instant specification has provided a written description for only a monomer comprising the amino acid sequence of SEQ ID NO:106, 107 or 108. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions on the claimed trimeric polypeptides comprising three monomers. Thus, the scope of the claims includes numerous structural variants of polypeptides, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what are the changes in the protein. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a polypeptide as recited in claim 1 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus of trimeric polypeptides.

Claim Rejections - 35 U.S.C. § 112, first paragraph, scope of enablement

2b. Claims 1, 18-23, 30, 35, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a trimeric polypeptide comprising three monomers, wherein each monomer comprises the amino acid sequence set forth in SEQ ID NO:106 or SEQ ID NO:7 or SEQ ID NO:8, and each monomer comprises a specific cytokine binding domain and a tetranectin trimerising domain wherein the tetranectin trimerising domain comprises the amino acid sequence of SEQ ID NO:81, does not reasonably provide enablement for as recited in claims 1, 18 and 19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 encompasses all monomers comprising a cytokine binding domain and a tetranectin trimerising domain. However, the instant specification has provided enablement for only a monomer comprising the amino acid sequence of SEQ ID NO:106 or SEQ ID NO:7 or SEQ ID NO:8. In addition, claim 18, for example, is overly broad in its limitation of "at least 87% identity" because no guidance is provided as to which of the myriad of polypeptide molecules encompassed by the claims will retain the characteristics of the desired polypeptide. Variants of a protein can be generated by deletions, insertions, and substitutions of amino acids, but no actual or prophetic examples on expected performance parameters of any of the possible variants of the claimed polypeptide molecule or muteins of the protein molecule have been disclosed. Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF)

protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate and use polypeptide having at least 87% amino acid sequence identity with SEQ ID NO:81, other than the polypeptide of SEQ ID NO:81 exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by

the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of the claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim rejections-35 U.S.C. 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35, line 3, is vague and indefinite because it recites "mutagenized to…" rather than the conventional "substituted with".

Claim rejections-Double Patenting

Non-statutory double patenting rejection (obviousness-type)

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4a. Claims 1, 18-20, 30, are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56-68 of copending Application No. 11/452,434 ('434). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 56-64, 80-81of copending Application No. 11/452,434 (having one common inventor with the instant application), claims a trimeric polypeptide complex comprising three monomer polypeptides, wherein (i) each of said monomer polypeptides comprises a tetranectin trimerising structural element (TTSE), said TTSE being a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in SEQ ID NO:40 and (ii) at least one of said monomer polypeptides is covalently linked to at least one heterologous moiety, where said at least one heterologous moiety is different from any of the fusion proteins CIIH6FXTN123, H6FXTN123, H6FXTN12, H6FCTN23, the

sequences of which are shown in SEQ ID NOs:24-27, and said complex remains as a trimer at a temperature of at least 60°C.

Instant claims 1, 18-23, 30, which claim a trimeric polypeptide comprising three monomers, wherein each monomer comprises a cytokine binding member domain and a tetranectin trimerising domain, are generic to claims 56-64, 80-81 in the '434 application and encompass subject matter to which the claims in the '434 application are a species because the claims in the instant application are of broader scope that the claims in the '434 application. However, the claims in the '434 application are obvious from the instant claims because the claims in the '434 application are directed to specific embodiments encompassed by instant claims 1, 18-23, 30. The product in the '434 application is included in instant claims 1, 18-23, 30. It would have been obvious to one of ordinary skill in the art at the time the present invention was made, that a trimeric polypeptide recited in instant claims included the trimeric polypeptide of the '434 application and encompassed the species claims in the '434 application. The claims of the '434 application if infringed upon would also result in infringement of the broad claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Claims 1, 18-23, 30, 35, are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
Primary Examiner
Art Unit 1646